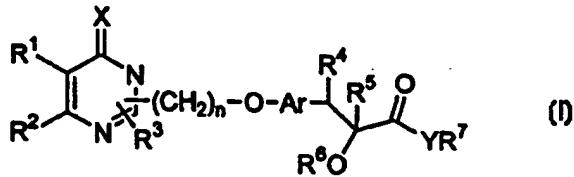


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(54) Title: NEW HETEROCYCLIC COMPOUNDS AND THEIR USE IN MEDICINE, PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM



(57) Abstract

The present invention relates to novel antiobesity and hypocholesterolemic compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. More particularly, the present invention relates to novel  $\beta$ -aryl- $\alpha$ -oxysubstituted alkylcarboxylic acids of general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them.

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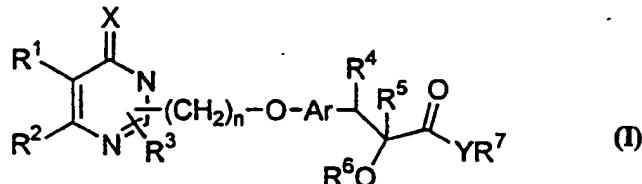
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## NEW HETEROCYCLIC COMPOUNDS AND THEIR USE IN MEDICINE, PROCESS FOR THEIR PREPARATION AND PHARMACEUTICAL COMPOSITIONS CONTAINING THEM

Field of Invention

5        The present invention relates to novel antiobesity and hypcholesterolemic compounds, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them. More particularly, the present invention relates to novel  $\beta$ -aryl- $\alpha$ -oxysubstituted alkylcarboxylic acids of the general formula (I), their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates and pharmaceutically acceptable compositions containing them.

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15        The present invention also relates to a process for the preparation of the above said novel compounds, their analogs, their derivatives, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, their pharmaceutically acceptable solvates, novel intermediates and pharmaceutical compositions containing them.

20        The compounds of the present invention lower total cholesterol (TC); increase high density lipoprotein (HDL) and decrease low density lipoprotein (LDL), which have beneficial effects on coronary heart disease and atherosclerosis.

25        The compounds of general formula (I) are useful in reducing body weight and for the treatment and/or prophylaxis of diseases such as hypertension, coronary heart disease, atherosclerosis, stroke, peripheral vascular diseases and related disorders. These compounds are useful for the treatment of familial hypercholesterolemia, hypertriglyceridemia, lowering of atherogenic lipoproteins, very low density lipoprotein (VLDL) and LDL. The compounds of the present invention can be used for the treatment of certain renal diseases including glomerulonephritis, glomerulosclerosis,

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nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, and nephropathy. The compounds of general formula (I) are also useful for the treatment/prophylaxis of insulin resistance (type II diabetes), leptin resistance, impaired glucose tolerance, dyslipidemia, disorders related to syndrome X such as hypertension, obesity, insulin resistance, coronary heart disease, and other cardiovascular disorders. These compounds may also be useful as aldose reductase inhibitors, for improving cognitive functions in dementia, treating diabetic complications, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), inflammatory bowel diseases, osteoporosis, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma and for the treatment of cancer. The compounds of the present inventions are useful in the treatment and/or prophylaxis of the above said diseases in combination/concomitant with one or more HMG CoA reductase inhibitors, and/or hypolipidemic/hypolipoproteinemic agents such as fibrin acid derivatives, nicotinic acid, cholestyramine, colestipol, or probucol.

15

#### Background of Invention

Atherosclerosis and other peripheral vascular diseases effect the quality of life of millions of people. Therefore, considerable attention has been directed towards understanding the etiology of hypercholesterolemia and hyperlipidemia and the development of effective therapeutic strategies.

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Hypercholesterolemia has been defined as plasma cholesterol level that exceeds arbitrarily defined value called "normal" level. Recently, it has been accepted that "ideal" plasma levels of cholesterol are much below the "normal" level of cholesterol in the general population and the risk of coronary artery disease (CAD) increases as cholesterol level rises above the "optimum" (or "ideal") value. There is 25 clearly a definite cause and effect-relationship between hypercholesterolemia and CAD, particularly for individuals with multiple risk factors. Most of the cholesterol is present in the esterified forms with various lipoproteins such as low density lipoprotein (LDL), intermediate density lipoprotein (IDL), high density lipoprotein (HDL) and partially as very low density lipoprotein (VLDL). Studies clearly indicate that there is 30 an inverse correlation between CAD and atherosclerosis with serum HDL-cholesterol concentrations. (Stampfer *et al.*, *N. Engl. J. Med.*, 325 (1991), 373-381) and the risk of CAD increases with increasing levels of LDL and VLDL.

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In CAD, generally "fatty streaks" in carotid, coronary and cerebral arteries, are found which are primarily free and esterified cholesterol. Miller *et al.*, (*Br. Med. J.*, 282 (1981), 1741-1744) have shown that increase in HDL-particles may decrease the number of sites of stenosis in coronary arteries of humans, and high level of HDL-cholesterol may protect against the progression of atherosclerosis. Picardo *et al.*, (*Arteriosclerosis* 6 (1986) 434 - 441) have shown by *in vitro* experiments that HDL is capable of removing cholesterol from cells. They suggest that HDL may deplete tissues of excess free cholesterol and transfer them to the liver (Macikinnon *et al.*, *J. Biol. Chem.* 261 (1986), 2548-2552). Therefore, agents that increase HDL cholesterol would have therapeutic significance for the treatment of hypercholesterolemia and coronary heart diseases (CHD).

Obesity is a disease highly prevalent in affluent societies and in the developing world and is a major cause of morbidity and mortality. It is a state of excess body fat accumulation. The causes of obesity are unclear. It is believed to be of genetic origin or promoted by an interaction between the genotype and environment. Irrespective of the cause, the result is fat deposition due to imbalance between the energy intake versus energy expenditure. Dieting, exercise and appetite suppression have been a part of obesity treatment. There is a need for efficient therapy to fight this disease since it may lead to coronary heart disease, diabetes, stroke, hyperlipidemia, gout, osteoarthritis, reduced fertility and many other psychological and social problems.

Diabetes and insulin resistance is yet another disease which severely effects the quality of life of a large population in the world. Insulin resistance is the diminished ability of insulin to exert its biological action across a broad range of concentrations. In insulin resistance, the body secretes abnormally high amounts of insulin to compensate for this defect; failing which, the plasma glucose concentration inevitably rises and develops into diabetes. Among the developed countries, diabetes mellitus is a common problem and is associated with a variety of abnormalities including obesity, hypertension, hyperlipidemia (*J. Clin. Invest.*, (1985) 75:809-817; *N. Engl. J. Med.* (1987) 317:350-357; *J. Clin. Endocrinol. Metab.*, (1988) 66 : 580 - 583; *J. Clin. Invest.*, (1975) 68:957-969) and other renal complications (See Patent Application No. WO 95/21608). It is now increasingly being recognized that insulin resistance and relative hyperinsulinemia have a contributory role in obesity, hypertension,

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atherosclerosis and type 2 diabetes mellitus. The association of insulin resistance with obesity, hypertension and angina has been described as a syndrome having insulin resistance as the central pathogenic link-Syndrome-X.

Hyperlipidemia is the primary cause of cardiovascular (CVD) and other peripheral vascular diseases. High risk of CVD is related to the higher LDL (Low Density Lipoprotein) and VLDL (Very Low Density Lipoprotein) seen in hyperlipidemia. Patients having glucose intolerance/insulin resistance in addition to hyperlipidemia have higher risk of CVD. Numerous studies in the past have shown that lowering of plasma triglycerides and total cholesterol, in particular LDL and VLDL and increasing HDL cholesterol help in preventing cardiovascular diseases.

Peroxisome proliferator activated receptors (PPAR) are members of the nuclear receptor super family. The gamma ( $\gamma$ ) isoform of PPAR (PPAR $\gamma$ ) has been implicated in regulating differentiation of adipocytes (Endocrinology, (1994) 135: 798-800) and energy homeostasis (Cell, (1995) 83: 803-812), whereas the alpha ( $\alpha$ ) isoform of PPAR (PPAR $\alpha$ ) mediates fatty acid oxidation (Trend. Endocrin. Metab., (1993) 4: 291-296) thereby resulting in reduction of circulating free fatty acid in plasma (Current Biol. (1995) 5: 618 -621). PPAR $\alpha$  agonists have been found useful for the treatment of obesity (WO 97/36579). It has been recently disclosed that the hypolipidaemic effect is enhanced when the molecule has both PPAR $\alpha$  and PPAR $\gamma$  agonist activity and suggested to be useful for the treatment of syndrome X (WO 97/25042). Synergism between the insulin sensitizer (PPAR $\gamma$  agonist) and HMG CoA reductase inhibitor has been observed which may be useful for the treatment of atherosclerosis and xanthoma. (EP 0 753 298).

It is known that PPAR $\gamma$  plays an important role in adipocyte differentiation (Cell, (1996) 87, 377-389). Ligand activation of PPAR is sufficient to cause complete terminal differentiation (Cell, (1994) 79, 1147-1156) including cell cycle withdrawal. PPAR $\gamma$  is consistently expressed in certain cells and activation of this nuclear receptor with PPAR $\gamma$  agonists would stimulate the terminal differentiation of adipocyte precursors and cause morphological and molecular changes characteristics of a more differentiated, less malignant state (Molecular Cell, (1998), 465-470; Carcinogenesis, (1998), 1949-53; Proc. Natl. Acad. Sci., (1997) 94, 237-241) and inhibition of

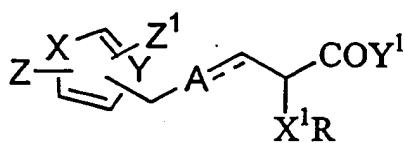
expression of prostate cancer tissue (Cancer Research (1998), 58:3344-3352). This would be useful in the treatment of certain types of cancer, which express PPAR $\gamma$  and could lead to a quite nontoxic chemotherapy.

Leptin resistance is a condition wherein the target cells are unable to respond to leptin signals. This may give rise to obesity due to excess food intake and reduced energy expenditure and cause impaired glucose tolerance, type 2 diabetes, cardiovascular diseases and such other interrelated complications. Kallen *et al* (Proc. Natl. Acad. Sci., (1996) 93, 5793-5796) have reported that insulin sensitizers which perhaps due to their PPAR agonist expression and lower plasma leptin concentrations.

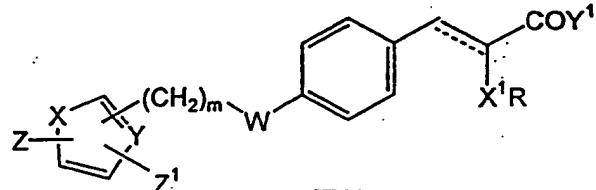
10 However, it has been recently disclosed that compounds having insulin sensitizing property also possess leptin sensitization activity. They lower the circulating plasma leptin concentrations by improving the target cell response to leptin (WO 98/02159).

15 A few  $\beta$ -aryl- $\alpha$ -hydroxy propionic acids, their derivatives, and their analogs have been reported to be useful in the treatment of hyperglycemia and hypercholesterolemia. Some of such compounds described in the prior art are outlined below:

i) U.S. Pat. 5,306,726 and WO 91/19702 disclose several 3-aryl-2-hydroxypropionic acid derivatives of general formula (IIa) and (IIb) as hypolipidemic and hypoglycemic agents.



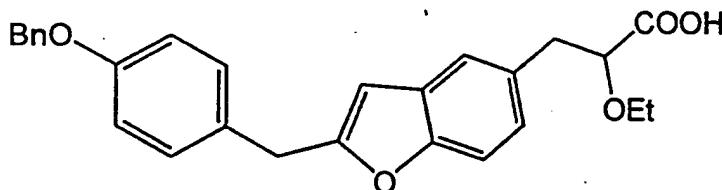
(II a)



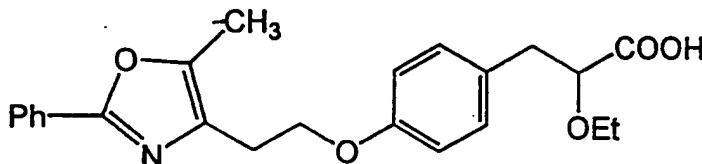
(II b)

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Examples of these compounds are shown in formula (II c) and (II d)



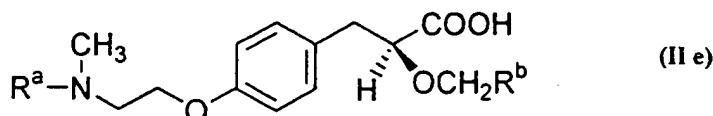
(II c)



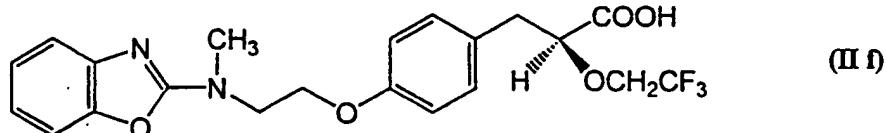
(II d)

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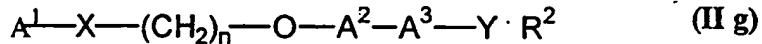
ii) International Patent Applications, WO 95/03038 and WO 96/04260 disclose compounds of formula (II e)



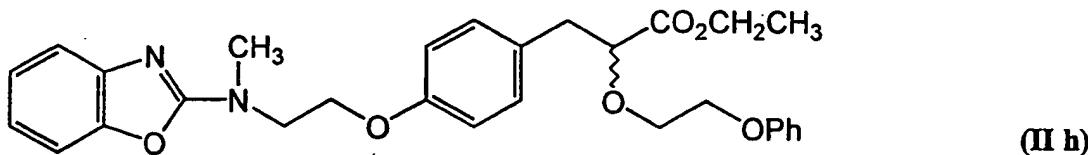
wherein  $R^a$  represents 2-benzoxazolyl or 2-pyridyl and  $R^b$  represent  $CF_3$ ,  $CH_2OCH_3$  or  $CH_3$ . A typical example is (S)-3-[4-[2-[N-(2-benzoxazolyl)N-methylamino]ethoxy]phenyl]-2-(2,2,2-trifluoroethoxy)propanoic acid (II f).



iii) International Patent Application Nos. WO 94/13650, WO 94/01420 and WO 95/17394 disclose the compounds of general formula (II g)



wherein  $A^1$  represent aromatic heterocycle,  $A^2$  represents substituted benzene ring and  $A^3$  represents moiety of formula  $(CH_2)_m-CH-(OR^1)$ , wherein  $R^1$  represents alkyl groups,  $m$  is an integer of 1-5;  $X$  represents substituted or unsubstituted N;  $Y$  represents C=O or C=S,  $R^2$  represents OR $^3$  where  $R^3$  may be hydrogen, alkyl, aralkyl, or aryl group and  $n$  is an integer of 2-6. An example of these compounds is shown in formula (II h)



#### Summary of the Invention

With an objective to develop novel compounds for lowering cholesterol and reducing body weight with beneficial effects in the treatment and/or prophylaxis of diseases related to increased levels of lipids, atherosclerosis, coronary artery diseases, Syndrome-X, impaired glucose tolerance, insulin resistance, insulin resistance leading to type 2 diabetes and diabetes complications thereof, for the treatment of diseases wherein insulin resistance is the pathophysiological mechanism, for the treatment and/

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or prophylaxis of leptin resistance and complications thereof, hypertension, atherosclerosis and coronary artery diseases with better efficacy, potency and lower toxicity, we focussed our research to develop new compounds effective in the treatment of above mentioned diseases. Effort in this direction has led to compounds 5 having general formula (I).

The main objective of the present invention is therefore, to provide novel  $\beta$ -aryl- $\alpha$ -oxysubstituted alkylcarboxylic acids, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, and their pharmaceutically acceptable solvates and pharmaceutical 10 compositions containing them, or their mixtures.

Another objective of the present invention is to provide novel  $\beta$ -aryl- $\alpha$ -oxy-substituted alkylcarboxylic acids, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, and their pharmaceutically acceptable solvates and pharmaceutical compositions 15 containing them or their mixtures which may have agonist activity against PPAR $\alpha$  and/or PPAR $\gamma$ , and may inhibit HMG CoA reductase, in addition to agonist activity against PPAR $\alpha$  and/or PPAR $\gamma$ .

Another objective of the present invention is to provide novel  $\beta$ -aryl- $\alpha$ -oxy-substituted alkylcarboxylic acids, derivatives, their analogs, their tautomeric forms, 20 their stereoisomers, their polymorphs, their pharmaceutically acceptable salts, and their pharmaceutically acceptable solvates and pharmaceutical compositions containing them or their mixtures having enhanced activities, without toxic effect or with reduced toxic effect.

Yet another objective of the present invention is to produce a process for the 25 preparation of novel  $\beta$ -aryl- $\alpha$ -oxysubstituted alkylcarboxylic acids of the formula (I) as defined above, their derivatives, their analogs, their tautomeric forms, their stereoisomers, their polymorphs, their pharmaceutically acceptable salts and their pharmaceutically acceptable solvates.

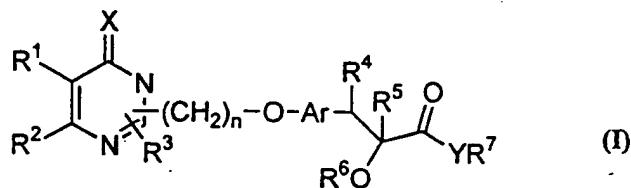
Still another objective of the present invention is to provide pharmaceutical 30 compositions containing compounds of the general formula (I), their analogs, their derivatives, their tautomers, their stereoisomers, their polymorphs, their salts, solvates

or their mixtures in combination with suitable carriers, solvents, diluents and other media normally employed in preparing such compositions.

A further objective of the present invention is to provide novel intermediates, a process for preparation of the intermediates and a process for the preparation of novel 5  $\beta$ -aryl- $\alpha$ -oxysubstituted alkylcarboxylic acids of formula (I), their derivatives, their analogs, their tautomers their stereoisomers, their polymorphs, their pharmaceutically acceptable salts and their pharmaceutically acceptable solvates using the intermediates.

Detailed Description of the Invention

10  $\beta$ -aryl  $\alpha$ -oxysubstituted propionic acids, their derivatives and their analogs of the present invention have the general formula (I)



where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when attached to the carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, 15 aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or two heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen 20 atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, mono alkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, 25

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alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by  $-(CH_2)_n-O-$  may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 – 4; Ar represents an unsubstituted or substituted divalent 5 single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> may be hydrogen, or unsubstituted or substituted groups 10 selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxy- carbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> may be hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, hetero- 15 aryl, or heteroaralkyl groups; Y represents oxygen or NR<sup>8</sup>, where R<sup>8</sup> represents hydrogen or unsubstituted or substituted groups selected from, alkyl, aryl, hydroxy- alkyl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; R<sup>7</sup> and R<sup>8</sup> together may form a substituted or unsubstituted 5 or 6 membered cyclic structure containing carbon atoms, which may optionally contain one or two heteroatoms selected from 20 oxygen, sulfur or nitrogen.

Suitable groups represented by R<sup>1</sup>, R<sup>2</sup> and the group R<sup>3</sup> when attached to carbon atom may be selected from hydrogen, halogen atom such as fluorine, chlorine, bromine, or iodine; hydroxy, cyano, nitro, formyl; substituted or unsubstituted (C<sub>1</sub>-C<sub>12</sub>)alkyl group, especially, linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, such as methyl, 25 ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, t-butyl, n-pentyl, iso-pentyl, hexyl and the like; cyclo(C<sub>3</sub>-C<sub>6</sub>)alkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like, the cycloalkyl group may be substituted; cyclo(C<sub>3</sub>-C<sub>6</sub>)alkoxy group such as cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy and the like, the cycloalkoxy group may be substituted; aryl group such as phenyl or naphthyl, the aryl group may be substituted; aralkyl such as benzyl or phenethyl, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, naphthylmethyl and the like, the aralkyl group may be substituted and the substituted 30 aralkyl is a group such as CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, Hal-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>,

CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub> and the like; heteroaryl group such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, tetrazolyl, benzopyranyl, benzofuranyl and the like, the heteroaryl group may be substituted; heterocyclyl groups such as aziridinyl, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl and the like, the heterocyclyl group may be substituted; aralkoxy group such as benzyloxy, phenethyloxy, naphthylmethyloxy, phenylpropyloxy and the like, the aralkoxy group may be substituted; heteroaralkyl group such as furanmethyl, pyridinemethyl, oxazolemethyl, oxazoleethyl and the like, the heteroaralkyl group may be substituted; aralkylamino group such as C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NH, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>NH, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NCH<sub>3</sub> and the like, which may be substituted; alkoxy carbonyl such as methoxycarbonyl or ethoxycarbonyl, which may be substituted; aryloxycarbonyl group such as unsubstituted or substituted phenoxy carbonyl, naphthylloxycarbonyl and the like; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethyloxycarbonyl, naphthylmethoxycarbonyl and the like, which may be substituted; (C<sub>1</sub>-C<sub>6</sub>)alkylamino group such as NHCH<sub>3</sub>, NHC<sub>2</sub>H<sub>5</sub>, NHC<sub>3</sub>H<sub>7</sub>, NHC<sub>6</sub>H<sub>13</sub> and the like; which may be substituted (C<sub>1</sub>-C<sub>6</sub>)dialkylamino group such as N(CH<sub>3</sub>)<sub>2</sub>, NCH<sub>3</sub>(C<sub>2</sub>H<sub>5</sub>); and the like, which may be substituted; alkoxyalkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl and the like, which may be substituted; aryloxyalkyl group such as C<sub>6</sub>H<sub>5</sub>OCH<sub>2</sub>, C<sub>6</sub>H<sub>5</sub>OCH<sub>2</sub>CH<sub>2</sub>, naphthylloxymethyl and the like, which may be substituted; 20 aralkoxyalkyl group such as C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>OCH<sub>2</sub>, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub> and the like, which may be substituted; heteroaryloxy and heteroaralkoxy, wherein heteroaryl and heteroaralkyl moieties are as defined earlier and may be substituted; aryloxy group such as phenoxy, naphthylloxy, the aryloxy group may be substituted; arylamino group such as HNC<sub>6</sub>H<sub>5</sub>, NCH<sub>3</sub>(C<sub>6</sub>H<sub>5</sub>), NHC<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>, NHC<sub>6</sub>H<sub>4</sub>-Hal and the like, which may be substituted; amino group which may be substituted; amino(C<sub>1</sub>-C<sub>6</sub>)alkyl which may be substituted; hydroxy(C<sub>1</sub>-C<sub>6</sub>)alkyl which may be substituted; (C<sub>1</sub>-C<sub>6</sub>)alkoxy such as methoxy, ethoxy, propyloxy, butyloxy, iso-propyloxy and the like, which may be substituted; thio(C<sub>1</sub>-C<sub>6</sub>)alkyl which may be substituted; (C<sub>1</sub>-C<sub>6</sub>)alkylthio which may be substituted; acyl group such as acetyl, propionyl or benzoyl, the acyl group may be substituted; acylamino groups such as NHCOCH<sub>3</sub>, NHCOC<sub>2</sub>H<sub>5</sub>, NHCOC<sub>3</sub>H<sub>7</sub>, NHCOC<sub>6</sub>H<sub>5</sub> which may be substituted; aralkoxycarbonylamino group such as NHCOOCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, NHCOOCH<sub>2</sub>CH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, N(CH<sub>3</sub>)COOCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>,

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N(C<sub>2</sub>H<sub>5</sub>)COOCH<sub>2</sub>C<sub>6</sub>H<sub>5</sub>, NHCOOCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>, NHCOOCH<sub>2</sub>C<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub> and the like, which may be substituted; aryloxycarbonylamino group such as NHCOOC<sub>6</sub>H<sub>5</sub>, NCH<sub>3</sub>COOC<sub>6</sub>H<sub>5</sub>, NC<sub>2</sub>H<sub>5</sub>COOC<sub>6</sub>H<sub>5</sub>, NHCOOC<sub>6</sub>H<sub>4</sub>CH<sub>3</sub>, NHCOOC<sub>6</sub>H<sub>4</sub>OCH<sub>3</sub> and the like which may be substituted; alkoxy carbonylamino group such as NHCOOC<sub>2</sub>H<sub>5</sub>,

5 NHCOOCH<sub>3</sub> and the like which may be substituted; carboxylic acid or its derivatives such as amides, like CONH<sub>2</sub>, CONHMe, CONMe<sub>2</sub>, CONHEt, CONEt<sub>2</sub>, CONHPh and the like, the carboxylic acid derivatives may be substituted; acyloxy group such as OOCMe, OOCEt, OOCPh and the like which may optionally be substituted; sulfonic acid or its derivatives such as SO<sub>2</sub>NH<sub>2</sub>, SO<sub>2</sub>NHMe, SO<sub>2</sub>NMe<sub>2</sub>, SO<sub>2</sub>NHCF<sub>3</sub> and the

10 like, the sulfonic acid derivatives may be substituted.

When the groups represented by R<sup>1</sup>, R<sup>2</sup> and the group R<sup>3</sup> when attached to carbon atom are substituted, the substituents may be selected from halogen, hydroxy, nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, aralkoxy, alkoxy carbonyl, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

It is preferred that the substituents on R<sup>1</sup> to R<sup>3</sup> represent halogen atom such as fluorine, chlorine, bromine; hydroxy group, optionally halogenated groups selected from alkyl group such as methyl, ethyl, isopropyl, n-propyl, or n-butyl; cycloalkyl group such as cyclopropyl; aryl group such as phenyl; aralkyl group such as benzyl; (C<sub>1</sub>-C<sub>3</sub>)alkoxy, benzyloxy, acyl or acyloxy groups.

Suitable cyclic structures formed by R<sup>1</sup> & R<sup>2</sup> together with the carbon atoms to which they are attached contain 5 to 6 ring atoms. The cyclic structure formed by R<sup>1</sup> and R<sup>2</sup> together with the carbon atoms to which they are attached may be a substituted or unsubstituted 5 or 6 membered cyclic structure containing carbon atoms which may optionally contain one or two heteroatoms selected from oxygen, nitrogen or sulfur. The cyclic structure may contain one or more double bonds. The cyclic structure may be optionally substituted phenyl, pyridyl, furanyl, thienyl, pyrrolyl and the like.

25 30 Suitable substituents on the cyclic structure formed by R<sup>1</sup> & R<sup>2</sup> together with the adjacent carbon atoms to which they are attached include hydroxy, halogen atom such

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as chlorine, bromine and iodine; nitro, cyano, amino, formyl, (C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy, thioalkyl, and alkylthio groups.

Suitable R<sup>3</sup> when attached to nitrogen atom is selected from hydrogen, hydroxy, formyl; substituted or unsubstituted (C<sub>1</sub>-C<sub>12</sub>)alkyl group, especially, linear or branched (C<sub>1</sub>-C<sub>6</sub>)alkyl group, such as methyl, ethyl, n-propyl, isopropyl, n-butyl, iso-butyl, t-butyl, n-pentyl, isopentyl, hexyl and the like; cyclo(C<sub>3</sub>-C<sub>6</sub>)alkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl and the like, the cycloalkyl group may be substituted; cyclo(C<sub>3</sub>-C<sub>6</sub>)alkoxy group such as cyclopropyloxy, cyclobutyloxy, cyclopentyloxy, cyclohexyloxy and the like, the cycloalkoxy group may be substituted; aryl group such as phenyl or naphthyl, the aryl group may be substituted; aralkyl such as benzyl or phenethyl, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>, naphthylmethyl and the like, the aralkyl group may be substituted and the substituted aralkyl is a group such as CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, Hal-C<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CH<sub>2</sub> and the like; heteroaryl group such as pyridyl, thienyl, furyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, tetrazolyl, benzopyranyl, benzofuranyl and the like, the heteroaryl group may be substituted; heterocyclyl groups such as aziridinyl, pyrrolidinyl, morpholinyl, piperidinyl, piperazinyl and the like, the heterocyclyl group may be substituted; aralkoxy group such as benzyloxy, phenethoxy, naphthylmethoxy, phenylpropyloxy and the like, the aralkoxy group may be substituted; heteroaralkyl group such as furanmethyl, pyridinemethyl, oxazolemethyl, oxazoleethyl and the like, the heteroaralkyl group may be substituted; aralkylamino group such as C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NH, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CH<sub>2</sub>NH, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>NCH<sub>3</sub> and the like, which may be substituted; alkoxy carbonyl such as methoxycarbonyl or ethoxycarbonyl which may be substituted; aryloxycarbonyl group such as unsubstituted or substituted phenoxy carbonyl, naphthyoxy carbonyl and the like; aralkoxycarbonyl group such as benzyloxycarbonyl, phenethyoxy carbonyl, naphthylmethoxycarbonyl and the like, which may be substituted; (C<sub>1</sub>-C<sub>6</sub>)alkylamino group such as NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, NCH<sub>3</sub>(C<sub>2</sub>H<sub>5</sub>), NHC<sub>2</sub>H<sub>5</sub>, NHC<sub>3</sub>H<sub>7</sub>, NHC<sub>6</sub>H<sub>13</sub> and the like, which may be substituted; (C<sub>1</sub>-C<sub>6</sub>)dialkylamino group N(CH<sub>3</sub>)<sub>2</sub>, NCH<sub>3</sub>(C<sub>2</sub>H<sub>5</sub>) and the like, which may be substituted; alkoxyalkyl group such as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl and the like, which may be substituted; aryloxyalkyl group such as C<sub>6</sub>H<sub>5</sub>OCH<sub>2</sub>, C<sub>6</sub>H<sub>5</sub>OCH<sub>2</sub>CH<sub>2</sub>, naphthyoxy methyl and the like, which may be substituted.

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substituted; aralkoxyalkyl group such as  $C_6H_5CH_2OCH_2$ ,  $C_6H_5CH_2OCH_2CH_2$  and the like, which may be substituted; heteroaryloxy and heteroaralkoxy, wherein the heteroaryl and the heteroaralkyl moieties are as defined earlier and may be substituted; aryloxy group such as phenoxy, naphthoxy, and the like the aryloxy group may be substituted; 5 arylamino group such as  $HNC_6H_5$ ,  $NCH_3(C_6H_5)$ ,  $NHC_6H_4CH_3$ ,  $NHC_6H_4Hal$  and the like, which may be substituted; amino group which may be substituted; amino( $C_1$ - $C_6$ )alkyl which may be substituted; hydroxy( $C_1$ - $C_6$ )alkyl which may be substituted; ( $C_1$ - $C_6$ )alkoxy such as methoxy, ethoxy, propyloxy, butyloxy, isopropyloxy and the like which may be substituted; thio( $C_1$ - $C_6$ )alkyl which may be substituted; ( $C_1$ - $C_6$ )alkylthio which may be substituted; acyl group such as acetyl, propionyl or benzoyl and the like, the acyl group may be substituted; acylamino groups such as  $NHCOCH_3$ ,  $NHCOC_2H_5$ ,  $NHCOC_3H_7$ ,  $NHCOC_6H_5$  which may be substituted; carboxylic acid derivatives such as amides, like  $CONH_2$ ,  $CONHMe$ ,  $CONMe_2$ ,  $CONHEt$ ,  $CONEt_2$ ,  $CONHPh$  and the like, the carboxylic acid derivatives 10 may be substituted; acyloxy group such as  $OOCMe$ ,  $OOCEt$ ,  $OOCPh$  and the like which may be substituted; sulfonic acid derivatives such as  $SO_2NH_2$ ,  $SO_2NHMe$ ,  $SO_2NMe_2$ ,  $SO_2NHCF_3$  and the like, the sulfonic acid derivatives may be substituted. 15

When the groups represented by  $R^3$  attached to nitrogen are substituted, preferred substituents may be selected from halogen such as fluorine, chlorine; 20 hydroxy, acyl, acyloxy, and amino groups.

$n$  is an integer ranging from 1-4. It is preferred that  $n$  be 1 or 2.

Suitable groups represented by  $Ar$  include substituted or unsubstituted groups selected from divalent phenylene, naphthylene, pyridyl, quinolinyl, benzofuryl, dihydrobenzofuryl, benzopyranyl, indolyl, indolinyl, azaindolyl, azaindolinyl, 25 pyrazolyl, benzothiazolyl, benzoxazolyl and the like. The substituents on the group represented by  $Ar$  may be selected from substituted or unsubstituted linear or branched ( $C_1$ - $C_6$ )alkyl, ( $C_1$ - $C_3$ )alkoxy, halogen, haloalkyl, haloalkoxy, acyl, amino, acylamino, thio or carboxylic or sulfonic acids and their derivatives.

It is preferred that  $Ar$  represents substituted or unsubstituted divalent 30 phenylene, naphthylene, benzofuryl, indolyl, indolinyl, quinolinyl, azaindolyl, azaindolinyl, benzothiazolyl or benzoxazolyl.

It is more preferred that Ar is represented by divalent phenylene or naphthylene, which may be unsubstituted or substituted by methyl, halomethyl, methoxy or halomethoxy groups.

Suitable R<sup>4</sup> includes hydrogen, lower alkyl groups such as methyl, ethyl or 5 propyl; hydroxy, (C<sub>1</sub>-C<sub>3</sub>)alkoxy; halogen atom such as fluorine, chlorine, bromine, or iodine; aralkyl such as benzyl, phenethyl, which may be unsubstituted or substituted or R<sup>4</sup> together with R<sup>5</sup> represent a bond.

Suitable R<sup>5</sup> may be hydrogen, lower alkyl groups such as methyl, ethyl or 10 propyl; hydroxy, (C<sub>1</sub>-C<sub>3</sub>)alkoxy; halogen atom such as fluorine, chlorine, bromine, iodine; acyl group such as linear or branched (C<sub>2</sub>-C<sub>10</sub>)acyl group such as acetyl, propanoyl, butanoyl, pentanoyl, benzoyl and the like; aralkyl such as benzyl, phenethyl, which may be unsubstituted or substituted or together with R<sup>4</sup> forms a bond.

When R<sup>4</sup> or R<sup>5</sup> represents substituted aralkyl, the preferred substituents are 15 hydroxy, halogen, alkyl and alkoxy.

It is preferred that R<sup>4</sup> and R<sup>5</sup> represent hydrogen atom or R<sup>4</sup> and R<sup>5</sup> together represent a bond.

Suitable groups represented by R<sup>6</sup> may be selected from hydrogen, substituted or unsubstituted, linear or branched (C<sub>1</sub>-C<sub>16</sub>)alkyl, preferably (C<sub>1</sub>-C<sub>12</sub>)alkyl group such 20 as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, pentyl, hexyl, octyl and the like; (C<sub>3</sub>-C<sub>7</sub>)cycloalkyl group such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, and the like, the cycloalkyl group may be substituted; aryl group such as phenyl, naphthyl, the aryl group may be substituted; heteroaryl group such as pyridyl, thienyl, furyl and the like, the heteroaryl group may be substituted; heteroaralkyl group such as furanmethyl, pyridinemethyl, oxazolemethyl, oxazoleethyl and the like, the heteroaralkyl group may be substituted; aralkyl group wherein the alkyl moiety may contain 25 C<sub>1</sub>-C<sub>6</sub> atoms such as benzyl and phenethyl etc, wherein the aryl moiety may be substituted; heterocyclyl group such as aziridinyl, pyrrolidinyl, piperidinyl and the like, the heterocyclyl group may be substituted; (C<sub>1</sub>-C<sub>6</sub>)alkoxy(C<sub>1</sub>-C<sub>6</sub>)alkyl group such 30 as methoxymethyl, ethoxymethyl, methoxyethyl, ethoxypropyl and the like, the alkoxyalkyl group may be substituted; substituted or unsubstituted, linear or branched (C<sub>2</sub>-C<sub>16</sub>)acyl group such as acetyl, propanoyl, butanoyl, benzoyl, octanoyl, decanoyl

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and the like; ( $C_1$ - $C_6$ )alkoxycarbonyl, the alkyl group may be substituted; aryloxy-carbonyl such as phenoxy carbonyl, naphthyl oxycarbonyl, the aryl group may be substituted; ( $C_1$ - $C_6$ )alkylaminocarbonyl, the alkyl group may be substituted; aryl-aminocarbonyl such as  $PhNHCO$ , or naphthylaminocarbonyl, the aryl moiety may be substituted. The substituents may be selected from halogen, hydroxy, or nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cyclo-alkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, alkoxy-carbonyl, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

Suitable groups represented by  $R^7$  may be selected from hydrogen, substituted or unsubstituted, linear or branched ( $C_1$ - $C_{16}$ )alkyl, preferably ( $C_1$ - $C_{12}$ )alkyl group such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, pentyl, hexyl, octyl and the like; ( $C_3$ - $C_7$ )cycloalkyl such as cyclopropyl, cyclopentyl, cyclohexyl and the like, the cycloalkyl group may be substituted; aryl group such as phenyl, naphthyl, the aryl group may be substituted; heteroaryl group such as pyridyl, thienyl, furyl and the like, the heteroaryl group may be substituted; heteroaralkyl group such as furanmethyl, pyridinemethyl, oxazolemethyl, oxazoleethyl and the like, the heteroaralkyl group may be substituted; aralkyl group such as benzyl and phenethyl, the aralkyl group may be substituted; heterocyclyl group such as aziridinyl, pyrrolidinyl, piperidinyl and the like, the heterocyclyl group may be substituted. The substituents on  $R^7$  may be selected from halogen, hydroxy, nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, aralkoxy, alkoxy carbonyl, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

Suitable groups represented by  $R^8$  may be selected from hydrogen, substituted or unsubstituted, linear or branched ( $C_1$ - $C_{16}$ )alkyl, preferably ( $C_1$ - $C_{12}$ )alkyl; hydroxy ( $C_1$ - $C_6$ )alkyl; aryl group such as phenyl, naphthyl; aralkyl group such as benzyl and phenethyl; heterocyclyl group such as aziridinyl, pyrrolidinyl, piperidinyl, and the like; heteroaryl group such as pyridyl, thienyl, furyl and the like; or heteroaralkyl group such as furanmethyl, pyridinemethyl, oxazolemethyl, oxazoleethyl and the like.

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5 The cyclic structure formed by R<sup>7</sup> and R<sup>8</sup> together with the carbon atoms to which they are attached may be a substituted or unsubstituted 5 or 6 membered cyclic structure containing carbon atoms which may optionally contain one or two hetero-atoms selected from oxygen, nitrogen or sulfur. The cyclic structure may contain one or more double bonds.

10 Suitable ring structures formed by R<sup>7</sup> and R<sup>8</sup> together may be selected from pyrrolidinyl, piperidinyl, morpholinyl, piperazinyl, oxazolinyl, diazolinyl and the like.

15 Suitable substituents on the cyclic structure formed by R<sup>7</sup> and R<sup>8</sup> taken together may be selected from halogen, hydroxy, alkyl, oxo, aralkyl and the like.

20 For any R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and Ar that may be substituted, the substituents are as defined above.

25 Suitable n is an integer ranging from 1 to 4, preferably n represents an integer 1 or 2.

15 The compounds of formula (I) where R<sup>6</sup> represents hydrogen atom and R<sup>7</sup> represents hydrogen or lower alkyl group have been claimed in our copending U.S. Patent Applications 08/777,627 and 08/884,816.

20 Pharmaceutically acceptable salts forming part of this invention include salts of the carboxylic acid moiety such as alkali metal salts like Li, Na, and K salts; alkaline earth metal salts like Ca and Mg salts; salts of organic bases such as lysine, arginine, guanidine, diethanolamine, choline, tromethamine and the like; ammonium or substituted ammonium salts and aluminum salts. Salts may include acid addition salts where appropriate which are, sulphates, nitrates, phosphates, perchlorates, borates, hydrohalides, acetates, tartrates, maleates, citrates, succinates, palmoates, methanesulphonates, benzoates, salicylates, hydroxynaphthoates, benzenesulfonates, ascorbates, glycerophosphates, ketoglutarates and the like. Pharmaceutically acceptable solvates may be hydrates or comprising other solvents of crystallization such as alcohols.

25 Particularly useful compounds according to the present invention includes:

30  $(\pm)$ -Ethyl 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

$(\pm)$ -2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

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( $\pm$ )-Sodium 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

[2R, N(1S)] 2-ethoxy-3-[4-[[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

5 [2S, N(1S)] 2-ethoxy-3-[4-[[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

(+)-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

(-)-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy] 10 phenyl]propanoic acid;

(-)-Sodium 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-(Morpholine-4-yl) 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2- quinazolinyl]methoxy]phenyl]propanamide;

15 ( $\pm$ )-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]-N-(2-fluorophenyl)propanamide;

( $\pm$ )-Ethyl 2-methoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Methoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy] 20 phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

25 [2S, N(1S)] 2-propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

[2R, N(1S)] 2-Propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

( $\pm$ )-Ethyl 2-(n-butoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] 30 methoxy]phenyl]propanoate;

( $\pm$ )-2-(n-Butoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-(n-octyloxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

5 ( $\pm$ )-Ethyl 2-benzyloxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl] propanoate;

( $\pm$ )-2-Benzylloxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

10 ( $\pm$ )-Ethyl 2-phenoxy 3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Phenoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl] propanoic acid;

( $\pm$ )-Ethyl 2-(2-methoxyethoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoate;

15 ( $\pm$ )-2-(2-Methoxyethoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoic acid;

20 [2R, N(1S)] 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

[2S, N(1S)] 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

25 (+)-2-Ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoic acid;

(-)-2-Ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoic acid;

(+)-Ethyl 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoate;

30

The blood samples were collected in fed state 1 hour after drug administration on 0 and 3 day of compound treatment. The blood was collected from the retro-orbital sinus through heparinised capillary in EDTA containing tubes. After centrifugation, plasma sample was separated for total cholesterol, HDL and triglyceride estimations.

5 Measurement of plasma triglyceride, total cholesterol and HDL were done using commercial kits (Dr. Reddy's Laboratory, Diagnostic Division, India). LDL and VLDL cholesterol were calculated from the data obtained for total cholesterol, HDL and triglyceride. The reduction of various parameters examined are calculated according to the formula.

Compound	Dose mg/kg	Triglyceride (%)↓	Total Cholesterol (%)↓	HDL↑ (%)	LDL (%)↓	VLDL(%)↓
Example 6	3 mg	45	11	NE	11	25
Example 15	10 mg	38	20	4	21	33

10

↓ = reduction; ↑ = increase; NE = no effect

c) Plasma triglyceride and total cholesterol lowering activity in Swiss albino mice and Guinea pigs

Male Swiss albino mice (SAM) and male Guinea pigs were obtained from NIN and housed in DRF animal house. All these animals were maintained under 12 hour light and dark cycle at  $25 \pm 1^{\circ}\text{C}$ . Animals were given standard laboratory chow (NIN, Hyderabad, India) and water, *ad libitum*. SAM of 20 - 25 g body weight range and Guinea pigs of 500 - 700 g body weight range were used (Oliver, P., Plancke, M. O., Marzin, D., Clavey, V., Sauzieres, J and Fruchart, J. C. Effects of fenofibrate, 20 gemfibrozil and nicotinic acid on plasma lipoprotein levels in normal and hyperlipidemic mice. Atherosclerosis. 1988. 70: 107-114).

25 The test compounds were administered orally to Swiss albino mice at 0.3 to 30 mg/kg/day dose for 6 days. Control mice were treated with vehicle (0.25% Carboxymethylcellulose; dose 10 ml/kg). The test compounds were administered orally to Guinea pigs at 0.3 to 30 mg/kg/day dose for 6 days. Control animals were treated with vehicle (0.25% Carboxymethylcellulose; dose 5 ml/kg).

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The blood samples were collected in fed state 1 hour after drug administration on 0 and 6 day of treatment. The blood was collected from the retro-orbital sinus through heparinised capillary in EDTA containing tubes. After centrifugation, plasma sample was separated for triglyceride and total cholesterol (Wieland, O. Methods of Enzymatic analysis. Bergmeyer, H. O., Ed., 1963. 211 - 214; Trinder, P. Ann. Clin. Biochem. 1969. 6 : 24 - 27). Measurement of plasma triglyceride, total cholesterol and HDL were done using commercial kits (Dr. Reddy's Diagnostic Division, Hyderabad, India).

Compound	Dose (mg / kg)	Triglyceride (%)↓
Example 42	3 mg	59
Example 35	1 mg	56
Example 28	10 mg	70
Example 40	10 mg	61
Example 64	10mg	57

**Formulae for calculation:**

10 1. Percent reduction in Blood sugar / triglycerides / total cholesterol were calculated according to the formula :

$$\text{Percent reduction (\%)} = \left[ 1 - \frac{\text{TT / OT}}{\text{TC / OC}} \right] \times 100$$

OC = Zero day control group value

OT = Zero day treated group value

15 TC = Test day control group value

TT = Test day treated group value

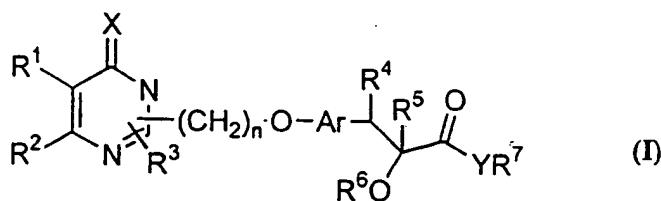
2. LDL and VLDL cholesterol levels were calculated according to the formula :

$$20 \text{ LDL cholesterol in mg/dl} = [ \text{Total cholesterol} - \text{HDL cholesterol} - \frac{\text{Triglyceride}}{5} ] \text{ mg/dl}$$

VLDL cholesterol in mg/dl=[Total cholesterol-HDL cholesterol-LDL cholesterol]  
mg/dl

CLAIMS

## 1. A compound of formula (I)



its derivatives, its analogs, its tautomeric forms, its stereoisomers, its polymorphs, its  
 5 pharmaceutically acceptable salts, and its pharmaceutically acceptable solvates,  
 wherein X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on  
 carbon atom, may be same or different and represent hydrogen, halogen, hydroxy,  
 nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cyclo-  
 alkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocycl, heteroaryl,  
 10 heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino,  
 acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl,  
 alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl,  
 aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino,  
 aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its  
 15 derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may  
 also form a 5-6 membered substituted or unsubstituted cyclic structure containing  
 carbon atoms with one or more double bonds, which may optionally contain one or  
 more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to  
 nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted  
 20 groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl,  
 heterocycl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino,  
 monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy,  
 aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy carbonyl, aryloxycarbonyl,  
 aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl  
 25 groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group  
 represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through  
 carbon atom where n is an integer ranging from 1 - 4; Ar represents an unsubstituted  
 or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents

hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents hydrogen, an

5 unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylamino- carbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl,

10 cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups and Y represents oxygen or NR<sup>8</sup>, where R<sup>8</sup> represents hydrogen, alkyl, aryl, hydroxyalkyl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; or R<sup>7</sup> and R<sup>8</sup> together may form a 5 or 6 membered cyclic structure containing carbon atoms, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen.

15 2. A compound of formula (I) according to claim 1, wherein the groups represented by R<sup>1</sup>, R<sup>2</sup> and the group R<sup>3</sup> when attached to carbon atom are substituted, the substituents are selected from halogen, hydroxy, or nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, aralkoxy, alkoxycarbonyl, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

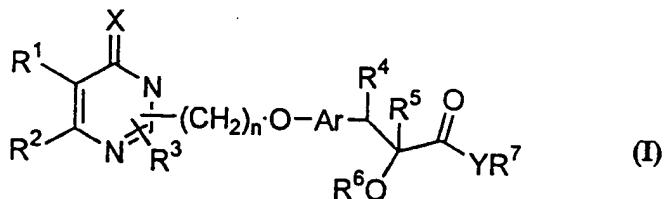
20 3. A compound of formula (I) according to claim 1 or 2, wherein substituents on the group R<sup>3</sup> when attached to nitrogen are selected from halogen, hydroxy, acyl, acyloxy, or amino groups.

25 4. A compound of formula (I) according to claim 1, 2 or 3, wherein Ar represents unsubstituted or substituted divalent phenylene, naphthylene, pyridyl, quinolinyl, benzofuryl, dihydrobenzofuryl, benzopyranyl, indolyl, indolinyl, azaindolyl, azaindolinyl, pyrazolyl, benzothiazolyl, or benzoxazolyl.

30 5. A compound of formula (I) according to claims 1, 2, 3 or 4, wherein substituents on the group represented by R<sup>6</sup> are selected from halogen, hydroxy, or nitro or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy,

cycloalkoxy, aryl, aralkyl, aralkoxyalkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, arylamino, aminoalkyl, aryloxy, alkoxy carbonyl, alkylamino, alkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid or its derivatives, or sulfonic acid or its derivatives.

5 6. A process for the preparation of compound of formula (I)

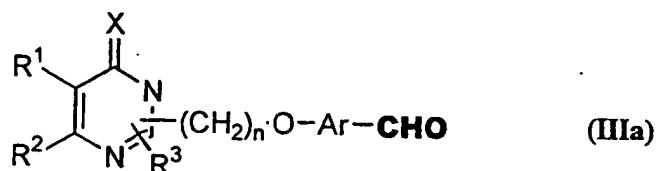


where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 – 4; Ar represents an unsubstituted

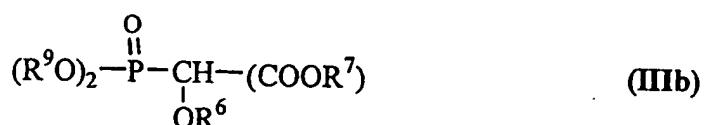
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or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> and R<sup>5</sup> together represent a bond; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocycl, heteroaryl, or heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocycl, heteroaryl, or heteroaralkyl groups and Y represents oxygen atom, which comprises:

10 a) reacting a compound of formula (IIIa)

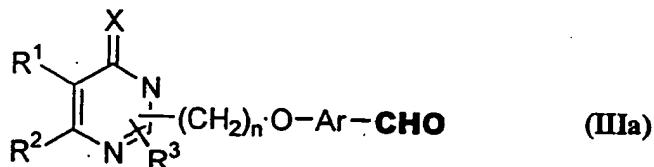


where all symbols are as defined above with a compound of formula (IIIb)



15 where R<sup>6</sup>, R<sup>7</sup> are as defined above excluding hydrogen and R<sup>9</sup> represents (C<sub>1</sub>-C<sub>6</sub>)alkyl, to yield compound of formula (I) defined above;

b) reacting the compound of formula (IIIa)



where all symbols are as defined earlier with Wittig reagents;

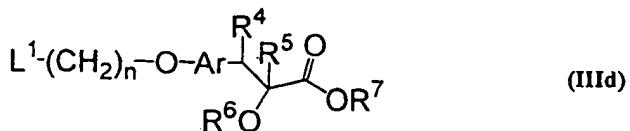
c) reacting a compound of formula (IIIc)



20

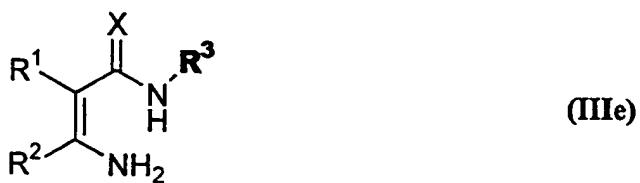
where all symbols are as defined above with a compound of formula (IIId)

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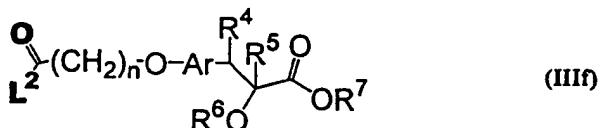


where  $\text{R}^4$ ,  $\text{R}^5$  together represent a bond, and all other symbols are as defined above and  $\text{L}^1$  is a leaving group to produce a compound of formula (I) defined above, where the linker group  $-(\text{CH}_2)_n-\text{O}-$  is attached to nitrogen atom ;

5 d) reacting a compound of formula (IIIe)

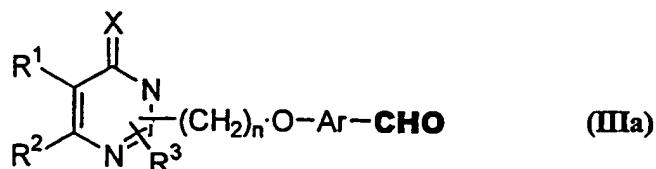


where all symbols are as defined above with a compound of formula (IIIf)



10 where  $\text{R}^4$ ,  $\text{R}^5$  together represent a bond,  $\text{L}^2$  is a leaving group and other symbols are as defined above, to produce a compound of formula (I) defined above , where the linker group  $-(\text{CH}_2)_n-\text{O}-$  is attached to carbon atom;

e) reacting a compound of formula (IIIa)



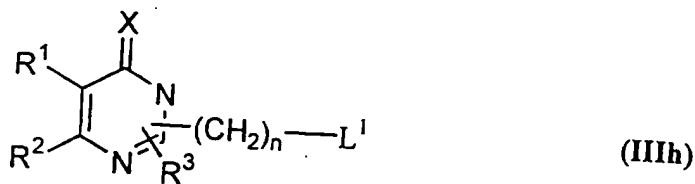
where all other symbols are as defined above with a compound of formula (IIIg)



15

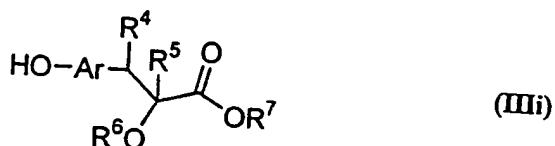
where  $\text{R}^5$  is hydrogen and all other symbols are as defined above to yield a compound of formula (I) as defined above after dehydration;

f) reacting a compound of formula (IIIh)



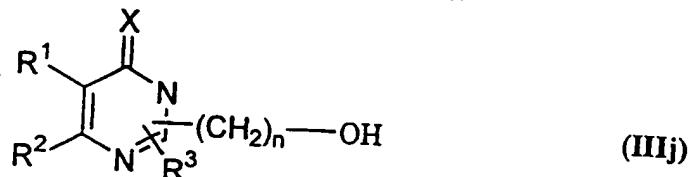
where all symbols are as defined earlier and  $L^1$  represents a leaving group, with compound of formula (IIIi)

5

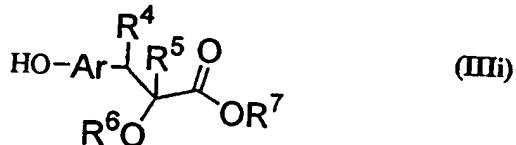


where  $R^4$  and  $R^5$  together represent a bond and all other symbols are as defined above to produce a compound of the formula (I) defined above;

g) reacting a compound of formula (IIIj)



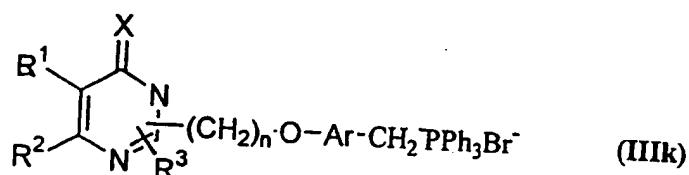
10 where all symbols are as defined above with a compound of general formula (IIIi)



where  $R^4$  and  $R^5$  together represent a bond and all other symbols are as defined above to produce a compound of formula (I) defined above;

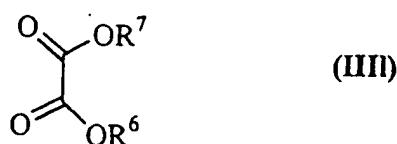
h) reacting a compound of formula (IIIk)

15



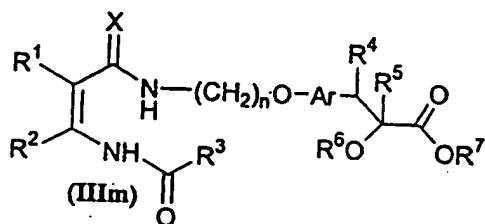
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where all symbols are as defined above with a compound of formula (III)



where  $R^6 = R^7$  and are as defined above excluding hydrogen to produce a compound of the formula (I);

5           i)     cyclising a compound of formula (III'm)



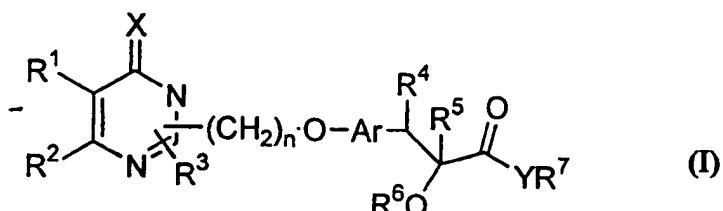
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where  $R^4$  and  $R^5$  together represent a bond,  $R^7$  is as defined above excluding hydrogen and all other symbols are as defined above to produce a compound of formula (I) defined above where the linking group  $-(CH_2)_n-O-$  is attached to nitrogen atom and if desired;

15           j)     converting the compounds of formula (I) obtained in any of the processes described above into pharmaceutically acceptable salts or pharmaceutically acceptable solvates.

7.     A process for the preparation of compound of formula (I)

20

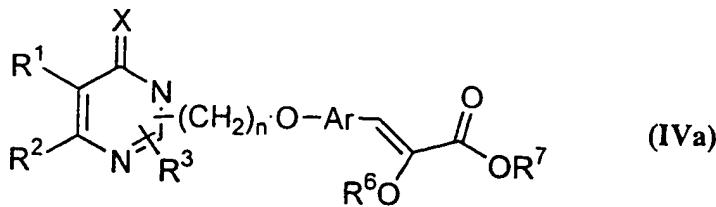


where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and the group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocycl, heteroaryl, 5 heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its 10 derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted 15 groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocycl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxy- carbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, 20 carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 – 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group; R<sup>5</sup> 25 represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl group; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocycl, heteroaryl, or heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen 30 when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl,

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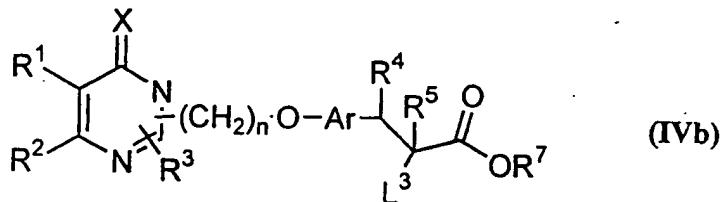
heterocyclyl, heteroaryl, or heteroaralkyl groups and Y represents oxygen atom, which comprises:

a) reducing a compound of formula (IVa)



5 where all symbols are as defined earlier, the compound of formula (IVa) represents a compound of formula (I) where  $R^4$  and  $R^5$  together represent a bond and Y represent oxygen atom and all other symbols are as defined above, to yield a compound of the formula (I) where  $R^4$  and  $R^5$  each represent hydrogen atom and all symbols are as defined above;

10 b) reacting a compound of formula (IVb)

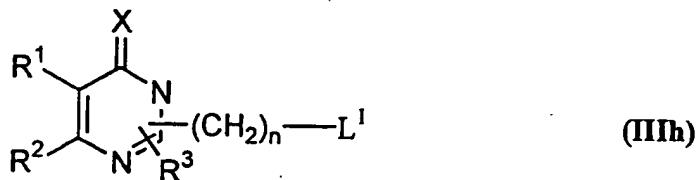


where all symbols are as defined above,  $R^7$  is as defined above excluding hydrogen and  $L^3$  is a leaving group with an alcohol of formula (IVc),



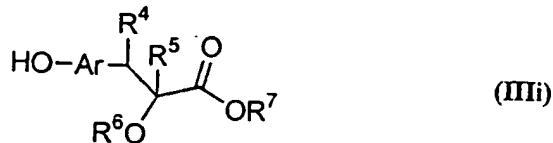
15 where  $R^6$  represents unsubstituted or substituted groups selected from alkyl, cyclo-alkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxy carbonyl, alkylamino-carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups to produce a compound of the formula (I) defined above;

c) reacting a compound of formula (IIIh)



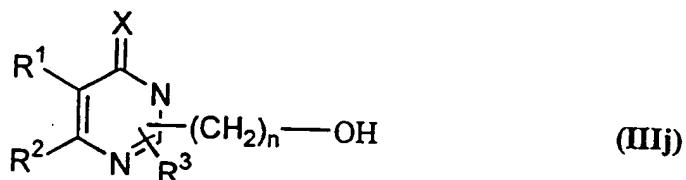
20 where  $L^1$  is a leaving group and all other symbols are as defined above with a compound of formula (IIIi)

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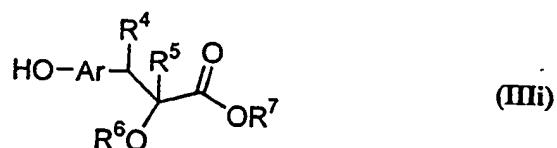
where all symbols are as defined earlier to produce a compound of the formula (I) defined above;

10 d) reacting a compound of formula (IIIj)



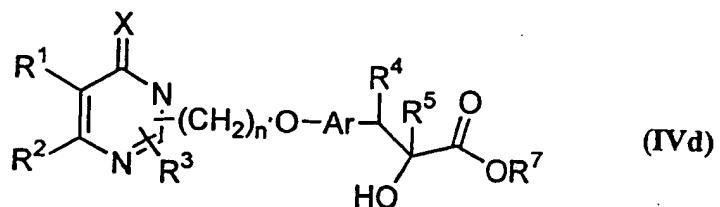
5

where all symbols are as defined above with a compound of formula (IIIi)



where all symbols are as defined earlier to produce a compound of the formula (I) defined above;

10 e) reacting a compound of formula (IVd)



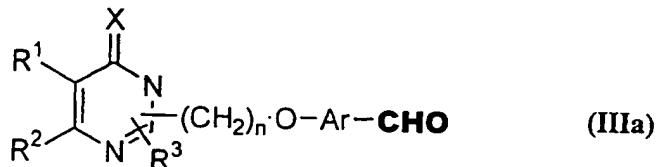
which represents a compound of formula (I) where R<sup>6</sup> represents hydrogen atom and all other symbols are as defined above with a compound of formula (IVe)



15 where R<sup>6</sup> represents unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups and L<sup>3</sup> is a leaving group to produce a compound of formula (I) defined above;

f) reacting a compound of the formula (IIIa)

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where all symbols are as defined above with a compound of formula (IIIg)

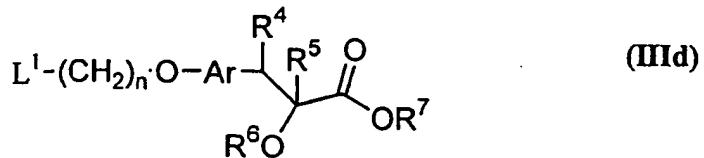


where  $R^5$  is hydrogen and all other symbols are as defined above to yield a compound of formula (I) as defined above after dehydroxylation;

g) reacting a compound of formula (IIIc)

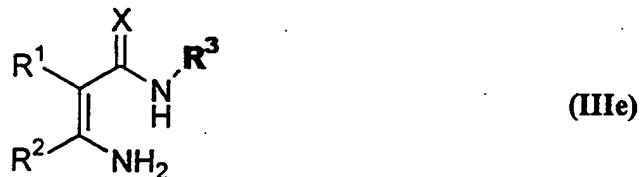


where all symbols are as defined above with a compound of formula (IIId)



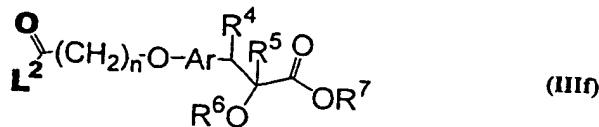
10 where  $L^1$  is a leaving group and all other symbols are as defined above to produce a compound of formula (I) defined above, where the linker group  $-(CH_2)_n-O-$  is attached to nitrogen atom;

h) reacting a compound of formula (IIIe)



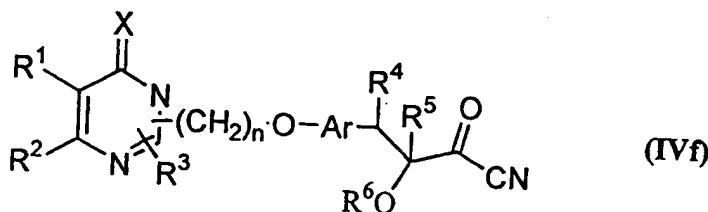
15 where all symbols are as defined above with a compound of formula (IIIe)

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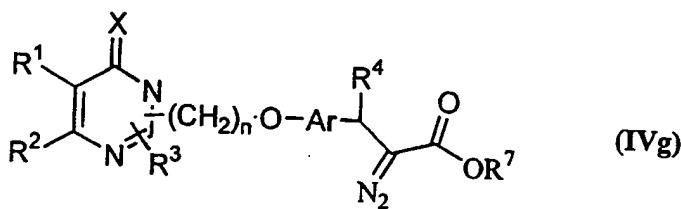
where all symbols are as defined above, and  $L^2$  is a leaving group to produce a compound of formula (I) defined above, where the linker group  $-(CH_2)_n-O-$  is attached to carbon atom;

5 i) converting a compound of formula (IVf)



where all symbols are as defined above to a compound of formula (I) defined above:

j) reacting a compound of formula (IV<sub>g</sub>)



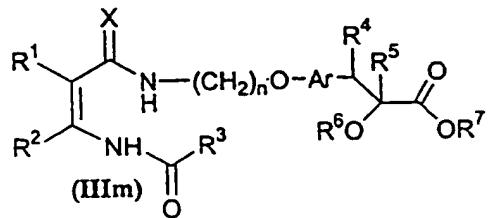
where R<sup>7</sup> is as defined above excluding hydrogen and all other symbols are as defined above with a compound of formula (IVc)



15 where  $R^6$  represents unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylamino-carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups to produce a compound of formula (I);

k) cyclising a compound of formula (III<sub>m</sub>)

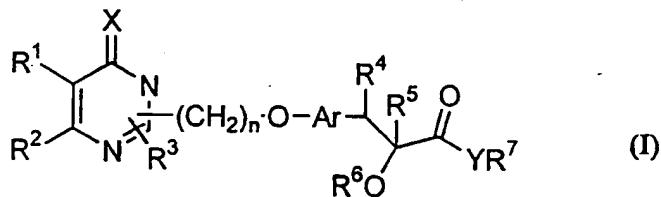
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where R<sup>7</sup> is as defined above excluding hydrogen and all other symbols are as defined  
 5 above to produce a compound of formula (I) defined above where the linking group –  
 (CH<sub>2</sub>)<sub>n</sub>-O- is attached to nitrogen atom and if desired;

1) converting the compounds of formula (I) obtained in any of the  
 processes described above into pharmaceutically acceptable salts or pharmaceutically  
 acceptable solvates.

10 8. A process for the preparation of compound of formula (I)

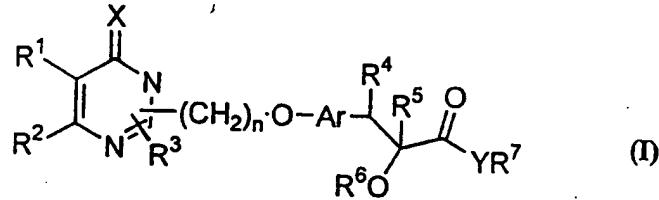


where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, 15 alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, 20 carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, 25 hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyl-

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oxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy-carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxy-alkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by  $-(CH_2)_n-O-$  may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 – 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy-carbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups, R<sup>7</sup> represents hydrogen and Y represents oxygen atom, which comprises: hydrolysing a compound of formula (I) described in any of the claims 6 and 7, where R<sup>7</sup> represents unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups and all other symbols are as defined earlier.

20 9. A process for the preparation of compound of formula (I)

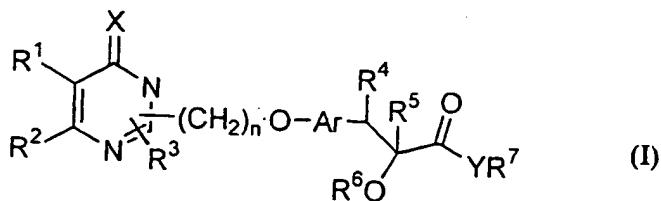


where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy-carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy-carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino,

carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from 5 oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyl-oxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy-10 carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxy-alkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 - 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or 15 heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, 20 cycloalkyl, aryl, aralkyl, alkoxyalkyl, aloxycarbonyl, aryloxycarbonyl, alkylamino-carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups 25 and Y represents NR<sup>8</sup>, where R<sup>8</sup> represents hydrogen, or unsubstituted or substituted alkyl, aryl, hydroxyalkyl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; or R<sup>7</sup> and R<sup>8</sup> together may form a 5 or 6 membered cyclic structure containing carbon atoms, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen, which comprises:

30 a) reacting a compound of formula (I)

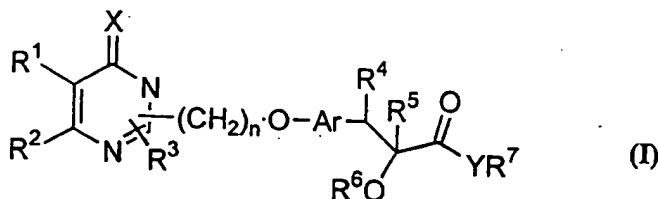
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where all symbols are as defined above and Y represents oxygen and R<sup>7</sup> represents hydrogen or a lower alkyl group or YR<sup>7</sup> represents a halogen atom, or COYR<sup>7</sup> represents a mixed anhydride group with appropriate amines of the formula NHR<sup>7</sup>R<sup>8</sup>,  
 5 where R<sup>7</sup> and R<sup>8</sup> are as defined earlier and if desired;

b) converting the compounds of formula (I) obtained above into pharmaceutically acceptable salts or pharmaceutically acceptable solvates.

10. A compound of formula (I)



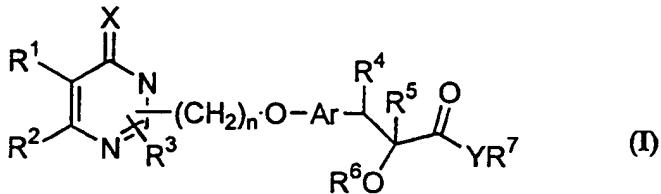
10 where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may form a 5-6 membered  
 15 substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy-  
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carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by  $-(CH_2)_n-O-$  may be attached either through nitrogen atom or through carbon atom where  $n$  is an integer ranging from 1 – 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group;  $R^4$  and  $R^5$  together represent a bond;  $R^6$  represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, aryloxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylamino-carbonyl, acyl, heterocycl, heteroaryl, or heteroaralkyl groups, with a provision that  $R^6$  does not represent hydrogen when  $R^7$  represents hydrogen or lower alkyl group;  $R^7$  represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocycl, heteroaryl, heteroaralkyl groups and Y represents oxygen atom, prepared according to the process of claim 6.

11. A compound of formula (I)

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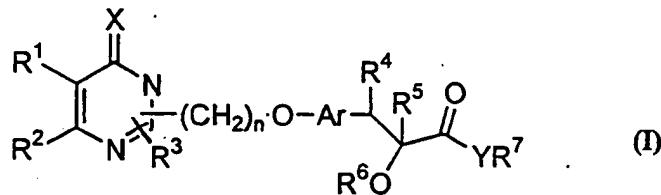


where X represents O or S; the groups  $R^1$ ,  $R^2$  and group  $R^3$  when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, 20 alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocycl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, 25 carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or  $R^1$ ,  $R^2$  along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from

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oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, 5 aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy-carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxy-alkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 - 10 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, or unsubstituted or substituted aralkyl group; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, or unsubstituted or substituted aralkyl; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cyclo- 15 alkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxycarbonyl, alkylamino-carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl 20 groups and Y represents oxygen atom, prepared according to the process of claim 7.

12. A compound of formula (I)

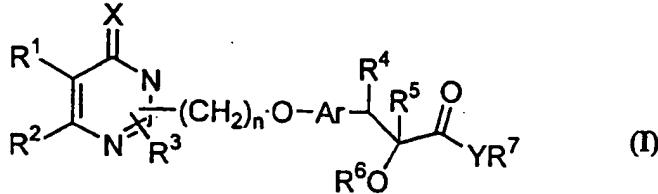


where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, 25 cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkyl-

thio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more 5 double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocycl, heteroaryl, heteroaralkyl, acyl, acyl-oxo, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, 10 aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy- carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxy- alkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 – 15 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; 20 R<sup>6</sup> represents unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxycarbonyl, alkylaminocarbonyl, aryl- aminocarbonyl, acyl, heterocycl, heteroaryl, or heteroaralkyl groups, R<sup>7</sup> represents hydrogen, and Y represents oxygen prepared according to the process of claim 8.

13. A compound of formula (I)

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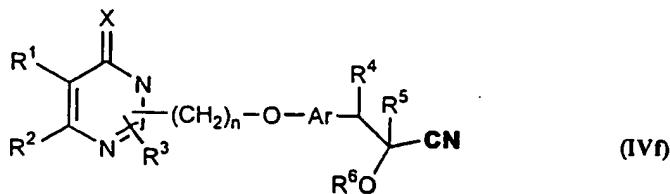


where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl,

alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 - 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxycarbonyl, alkylamino carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups, with a provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups and Y represents NR<sup>8</sup>, where R<sup>8</sup> represents hydrogen, or unsubstituted or substituted alkyl, aryl, hydroxyalkyl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; R<sup>7</sup> and R<sup>8</sup> together may form a 5 or 6 membered cyclic structure containing

carbon atoms, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen, prepared according to the process of claim 9.

14. An intermediate of formula (IVf)



5 where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocycl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may form a 5-6 membered

10 substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocycl, heteroaryl, heteroaralkyl, acyl, acyl- oxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy- carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxy- alkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either

15 through nitrogen atom or through carbon atom where n is an integer ranging from 1 - 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl

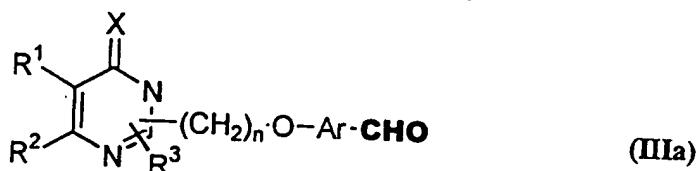
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group, acyl, unsubstituted or substituted aralkyl or  $R^5$  forms a bond together with  $R^4$ ;  $R^6$  represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxycarbonyl, alkylamino-carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaromatic.

5 15. A process for the preparation of the intermediate of formula (IVf) defined in  
claim 14, which comprises:

a) reacting a compound of formula (IIIa)



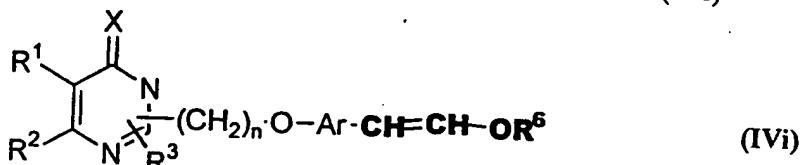
where all symbols are as defined in claim 14 with a compound of formula (IVh)

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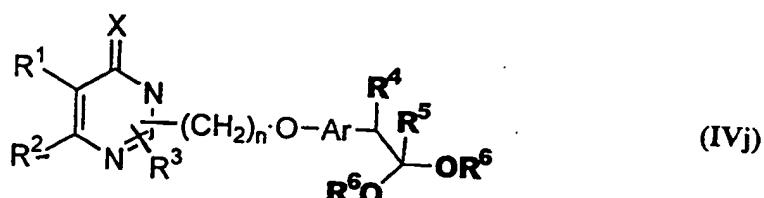
where  $R^6$  represents unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylamino-carbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl group and Hal represents a halogen atom, to yield a compound of formula (IVi)

15



where all symbols are as defined above

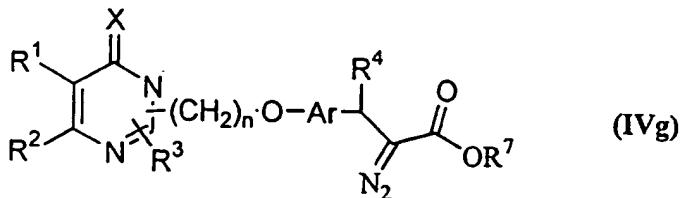
b) reacting the compound of formula (IVi) with an alcohol of the formula  $R^6OH$  where  $R^6$  is unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups to yield a compound of formula (IVj).



where  $R^6$  is as defined above and all other symbols are as defined earlier.

c) reacting the compound of formula (IVj) obtained above where all symbols are as defined above with trialkylsilyl cyanide to produce a compound of formula (IVf) where all symbols are as defined above.

16. An intermediate of formula (IVg)



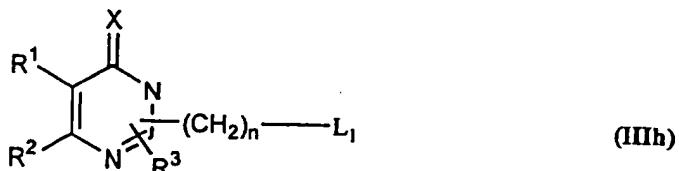
where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when present on carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocycl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonyl amino, aryloxycarbonyl amino, aralkoxycarbonyl amino, carboxylic acid or its derivatives, or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, heterocycl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom where n is an integer ranging from 1 - 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower

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alkyl, unsubstituted or substituted aralkyl; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups.

17. A process for the preparation of the intermediate of formula (IVg) as defined in  
5 claim 16, which comprises:

a) reacting a compound of formula (IIIh)

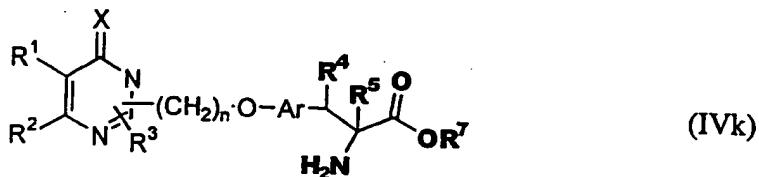


where L<sup>1</sup> is a leaving group and all other symbols are as defined above with a compound of formula (IVl)



10

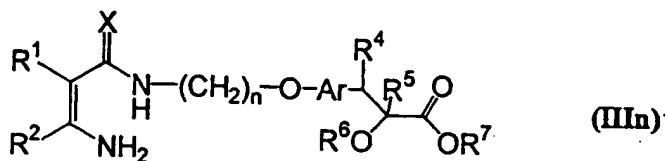
where R<sup>5</sup> is hydrogen atom and all other symbols are as defined above, to yield a compound of formula (IVk)



15

where R<sup>5</sup> is hydrogen atom and all other symbols are as defined above, and  
b) reacting a compound of formula (IVk) obtained above with an diazotizing agent.

18. An intermediate of formula (IIIln)



20 where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl,

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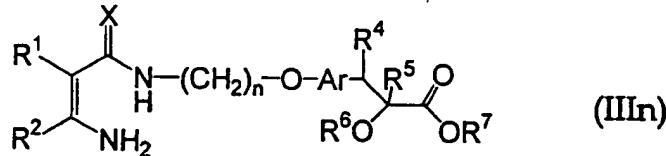
acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxycarbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives, or

5 sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may also form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more heteroatoms selected from oxygen, nitrogen and sulfur; n is an integer ranging from 1 – 4; Ar represents an unsubstituted or substituted

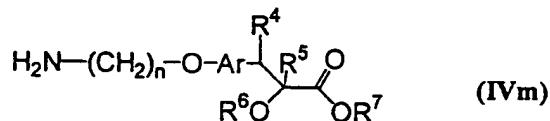
10 divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted

15 groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, aryloxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups.

20 19. A process for the preparation of the intermediate of formula (IIIIn) defined in claim 18,



which comprises reacting a compound of formula (IVm)



25 where all symbols are as defined in claim 18 with a compound of formula (IVo)

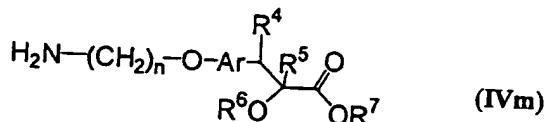
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where  $R^1$ ,  $R^2$  and  $X$  are as defined earlier to produce a compound of formula (IIIn) defined above.

20. An intermediate of formula (IVm)

5

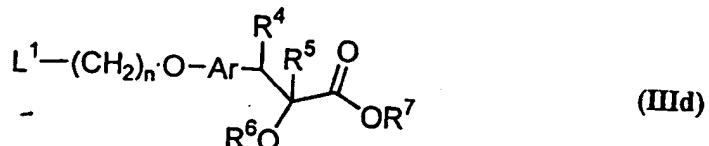


where  $n$  is an integer ranging from 1 – 4;  $Ar$  represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group;  $R^4$  represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group  $R^5$ ;  $R^5$  represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or  $R^5$  forms a bond together with  $R^4$ ;  $R^6$  represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups;  $R^7$  represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups.

10 21. A process for the preparation of the intermediate of formula (IVm) defined in claim 20,

15 20 which comprises

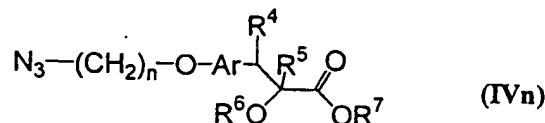
a) preparing from a compound of formula (IIId)



where  $L^1$  is a leaving group and all other symbols are as defined earlier by Gabriel synthesis;

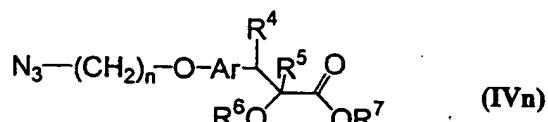
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## b) reducing a compound of formula (IVn)



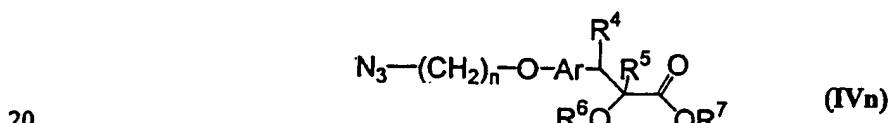
where R<sup>4</sup> and R<sup>5</sup> represent hydrogen atom and all other symbols are as defined earlier.

## 5 22. An intermediate of formula (IVn)



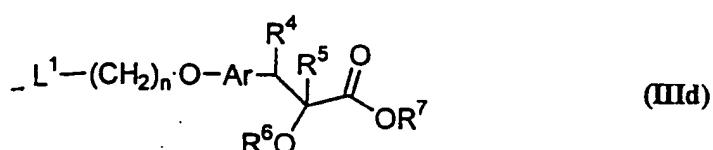
where n is an integer ranging from 1 – 4; Ar represents an unsubstituted or substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or 10 forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxycarbonyl, aryloxycarbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, hetero- 15 aryl, or heteroaralkyl groups; and R<sup>7</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl groups.

## 23. A process for the preparation of the intermediate of formula (IVn) defined in claim in 22,



20 which comprises:

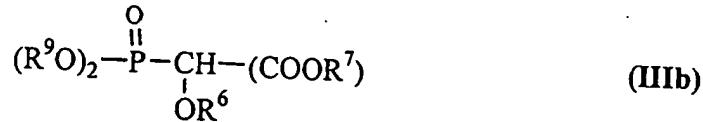
## a) treating a compound of formula (IIId)



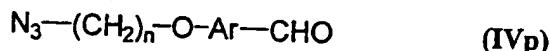
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where  $L^1$  is a leaving group and all symbols are as defined in claim 22, with appropriate azides to yield the compound of the formula (IVn);

b) reacting a compound of formula (IIIb)



5. where  $R^6$ ,  $R^7$  are as defined earlier excluding hydrogen and  $R^9$  represents  $(C_1-C_6)$ alkyl with a compound of formula (IVp)



where all symbols are as defined earlier by to yield a compound of the formula (IVn).

24. A compound according to claim 1 which is selected from:

10 (±)-Ethyl 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

(±)-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

15 (±)-Sodium 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

[2R, N(1S)] 2-ethoxy-3-[4-[[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl] -N-(2-hydroxy-1-phenylethyl)propanamide;

[2S, N(1S)] 2-ethoxy-3-[4-[[3-Methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

20 (+)-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

(-)-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

25 (-)-Sodium 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

(±)-(Morpholine-4-yl) 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanamide;

(±)-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]-N-(2-fluorophenyl)propanamide;

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( $\pm$ )-Ethyl 2-methoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Methoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

5 ( $\pm$ )-Ethyl 2-propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

[2S, N(1S)] 2-propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] 10 methoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

[2R, N(1S)] 2-Propoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

( $\pm$ )-Ethyl 2-(n-butoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoate;

15 ( $\pm$ )-2-(n-Butoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-(n-octyloxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] 20 methoxy]phenyl]propanoate;

( $\pm$ )-Ethyl 2-benzyloxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Benzylxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-phenoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] 25 methoxy]phenyl]propanoate;

( $\pm$ )-2-Phenoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-(2-methoxyethoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2- 30 quinazolinyl]methoxy]phenyl]propanoate;

( $\pm$ )-2-(2-Methoxyethoxy)-3-[4-[[3-methyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

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( $\pm$ )-Ethyl 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl] propanoic acid;

5 [2R, N(1S)] 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

[2S, N(1S)] 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

(+)-2-Ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoic acid;

(-)-2-Ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoic acid;

(+)-Ethyl 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoate;

15 (-)-Ethyl 2-ethoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]propanoate;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoic acid;

[2R, N(1S)] 2-ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

[2S, N(1S)] 2-ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]-N-(2-hydroxy-1-phenylethyl)propanamide;

25 (+)-2-Ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy] phenyl]propanoic acid;

(-)-2-Ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoic acid;

(+)-Ethyl 2-ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]propanoate;

30 (-)-Ethyl 2-ethoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]propanoate;

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( $\pm$ )-Ethyl 2-ethoxy-3-[4-[2-[4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl] propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[2-[4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy]phenyl] propanoic acid;

5 ( $\pm$ )-Ethyl 2-phenoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]propanoate;

( $\pm$ )-2-Phenoxy-3-[4-[2-[2-ethyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoic acid;

10 ( $\pm$ )-Ethyl 2-phenoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl] ethoxy]phenyl]propanoate;

( $\pm$ )-2-Phenoxy-3-[4-[2-[2-methyl-4-oxo-3,4-dihydro-3-quinazolinyl]ethoxy] phenyl]propanoic acid;

15 ( $\pm$ )-Ethyl 2-ethoxy-3-[4-[2-[2-ethyl-4-methyl-6-oxo-1-pyrimidinyl] ethoxy] phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[2-[2-ethyl-4-methyl-6-oxo-1-pyrimidinyl]ethoxy] phenyl] propanoic acid;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-phenyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

20 ( $\pm$ )-2-Ethoxy-3-[4-[2-[2-ethyl-4-methyl-6-oxo-1-pyrimidinyl]ethoxy] phenyl] propanoic acid;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-phenyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[[3-phenyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy] phenyl]propanoic acid;

25 ( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-6,7-dimethoxy-2-quinazolinyl]methoxy]phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[[3-methyl-4-oxo-3,4-dihydro-6,7-dimethoxy-2-quinazolinyl]methoxy] phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-(4-methylphenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy] phenyl]propanoate;

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( $\pm$ )-2-Ethoxy-3-[4-[[3-(4-methylphenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-(4-methoxyphenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy] phenyl]propanoate;

5 ( $\pm$ )-2-Ethoxy-3-[4-[[3-(4-methoxyphenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoic acid;

( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-benzyl-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoate;

10 ( $\pm$ )-2-Ethoxy-3-[4-[[3-benzyl-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid;

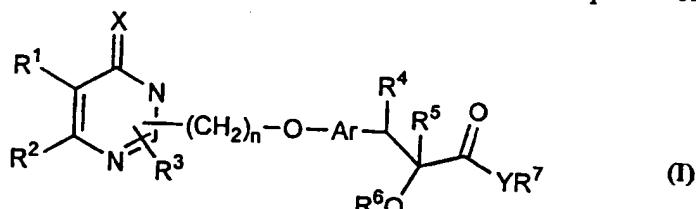
( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-(3-chlorophenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[[3-(3-chlorophenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoic acid;

15 ( $\pm$ )-Ethyl 2-ethoxy-3-[4-[[3-(3-chloro-4-fluorophenyl)-4-oxo-3,4-dihydro-2-quinazolinyl]methoxy]phenyl]propanoate;

( $\pm$ )-2-Ethoxy-3-[4-[[3-(3-chloro-4-fluorophenyl)-4-oxo-3,4-dihydro-2-quinazolinyl] methoxy]phenyl]propanoic acid.

25. A pharmaceutical composition which comprises a compound of formula (I)



20

as defined in claims 1-5, 10-13, or 24 and a pharmaceutically acceptable carrier, diluent, excipient or solvate.

26. A pharmaceutical composition as claimed in claim 25, in the form of a tablet, capsule, powder, syrup, solution or suspension.

25 27. A method of preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism comprising administering a compound of formula (I) as defined in claims

1-5, 10-13 or 24 or a compound as claimed in claim 24 or a pharmaceutical composition as claimed in claims 25 and 26 to a patient in need thereof.

28. A method according to claim 27, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as 5 hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving 10 cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

29. A method according to claim 28, for the treatment or prophylaxis of disorders related to Syndrome X, which comprises administering an agonist of PPAR $\alpha$  and/or 15 PPAR $\gamma$  of formula (I).

30. A method of reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma comprising an effective amount of compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claims 25 and 26 to a patient in need thereof.

20 31. A method of preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism comprising administering a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claim 25 and 25 26 in combination/concomitant with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol which may be administered together or within such a period as to act synergistically together to a patient in need thereof.

32. A method according to claim 31, wherein the disease is type II diabetes, 30 impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis,

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glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

33. A method according to claim 32, for the treatment or prophylaxis of disorders related to Syndrome X, which comprises administering a compound of formula (I) in combination with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol which may be administered together or within such a period as to act synergistically together.

34. A method of reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma, which comprises administering a compound of formula (I) claimed in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claims 25 and 26 in combination/concomitant with HMG CoA reductase inhibitors or fibrates or nicotinic acid or cholestyramine or colestipol or probucol which may be administered together or within such a period as to act synergistically together to a patient in need thereof.

35. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13, or 24 for preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism.

36. Use according to claim 35, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

37. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 for reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma comprising an effective amount of compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as 5 claimed in claims 25 and 26 to a patient in need thereof.

38. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24, in combination/concomitant with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol which may be administered together or within such a period as to act synergistically together for preventing or 10 treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism to a patient in need thereof.

39. Use according to claim 38, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as 15 hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive functions in dementia and treating diabetic complications, osteoporosis, 20 inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

40. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 in combination/concomitant with HMG CoA reductase inhibitors, fibrates, 25 nicotinic acid, cholestyramine, colestipol or probucol for reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL or free fatty acids in the plasma.

41. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24, for preparing a medicament for preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin 30 resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism.

42. Use according to claim 41, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

5 43. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 for preparing a medicament for reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma.

10 44. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 for preparing a medicament in combination/concomitant with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol for preventing or treating hypolipidemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism.

15 45. Use according to claim 44, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

20 46. Use of a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 for preparing a medicament in combination/concomitant with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol for reducing

plasma glucose, triglycerides, total cholesterol, LDL, VLDL or free fatty acids in the plasma.

47. A medicine for preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism comprising administering a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claims 25 and 26.

48. A medicine according to claim 47, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

49. A medicine for reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma comprising an effective amount of compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claims 25 and 26.

50. A medicine for preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism comprising a compound of formula (I) as defined in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claims 25 and 26 and HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol.

51. A medicine according to claim 50, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipidaemia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and

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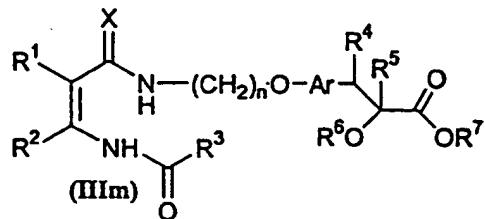
other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving

5 cognitive functions in dementia and treating diabetic complications, osteoporosis, inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

52. A medicine for reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma, which comprises a compound of formula (I) 10 claimed in any one of claims 1-5, 10-13 or 24 or a pharmaceutical composition as claimed in claims 25 and 26 and HMG CoA reductase inhibitors, fibrate, nicotinic acid, cholestyramine, colestipol or probucol.

53. An intermediate of formula (III<sup>m</sup>)

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where X represents O or S; the groups R<sup>1</sup>, R<sup>2</sup> and group R<sup>3</sup> when attached to the carbon atom, may be same or different and represent hydrogen, halogen, hydroxy, nitro, cyano, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aryloxy, aralkyl, aralkoxy, heterocyclyl, heteroaryl, 25 heteroaralkyl, heteroaryloxy, heteroaralkoxy, acyl, acyloxy, hydroxyalkyl, amino, acylamino, monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, alkoxy carbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl, alkoxy carbonylamino, aryloxycarbonylamino, aralkoxycarbonylamino, carboxylic acid or its derivatives or sulfonic acid or its derivatives; or R<sup>1</sup>, R<sup>2</sup> along with the adjacent atoms to which they are attached may 30 form a 5-6 membered substituted or unsubstituted cyclic structure containing carbon atoms with one or more double bonds, which may optionally contain one or more

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heteroatoms selected from oxygen, nitrogen and sulfur; R<sup>3</sup> when attached to nitrogen atom represents hydrogen, hydroxy, formyl or unsubstituted or substituted groups selected from alkyl, cycloalkyl, alkoxy, cycloalkoxy, aryl, aralkyl, hetero-cyclyl, heteroaryl, heteroaralkyl, acyl, acyloxy, hydroxyalkyl, amino, acylamino,

5 monoalkylamino, dialkylamino, arylamino, aralkylamino, aminoalkyl, aryloxy, aralkoxy, heteroaryloxy, heteroaralkoxy, alkoxy carbonyl, aryloxy carbonyl, aralkoxy carbonyl, alkoxyalkyl, aryloxyalkyl, aralkoxyalkyl, alkylthio, thioalkyl groups, carboxylic acid derivatives, or sulfonic acid derivatives; the linking group represented by -(CH<sub>2</sub>)<sub>n</sub>-O- may be attached either through nitrogen atom or through carbon atom

10 where n is an integer ranging from 1-4; Ar represents an optionally substituted divalent single or fused aromatic or heterocyclic group; R<sup>4</sup> represents hydrogen atom, hydroxy, alkoxy, halogen, lower alkyl, unsubstituted or substituted aralkyl group or forms a bond together with the adjacent group R<sup>5</sup>; R<sup>5</sup> represents hydrogen, hydroxy, alkoxy, halogen, lower alkyl group, acyl, unsubstituted or substituted aralkyl or R<sup>5</sup> forms a bond together with R<sup>4</sup>; R<sup>6</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, alkoxyalkyl, alkoxy carbonyl, aryloxy carbonyl, alkylaminocarbonyl, arylaminocarbonyl, acyl, heterocyclyl, heteroaryl, or heteroaralkyl groups, with the provision that R<sup>6</sup> does not represent hydrogen when R<sup>7</sup> represents hydrogen or lower alkyl group; R<sup>7</sup> represents hydrogen or unsubstituted or substituted groups selected from alkyl, cycloalkyl, aryl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; Y represents oxygen or NR<sup>8</sup>, where R<sup>8</sup> represents hydrogen, or unsubstituted or substituted groups selected from alkyl, aryl, hydroxyalkyl, aralkyl, heterocyclyl, heteroaryl, or heteroaralkyl groups; or R<sup>7</sup> and R<sup>8</sup> together may form a substituted or unsubstituted 5 or 6 membered cyclic structure containing

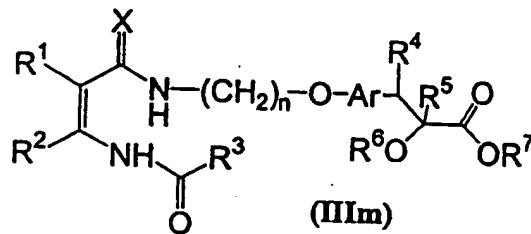
15 carbon atoms, which may optionally contain one or more heteroatoms selected from oxygen, sulfur or nitrogen.

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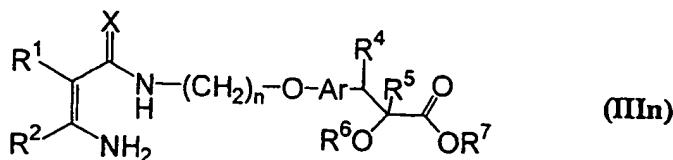
54. A process for the preparation of the intermediate of formula (IIIm) defined in claim 53

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which comprises reacting a compound of formula (IIIn)



where all symbols are as defined above, with a compound of formula (IIIo)

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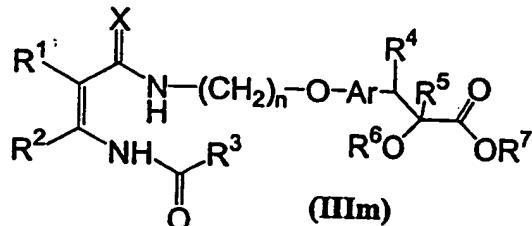


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where  $L^2$  is a leaving group and all other symbols are as defined above, to produce a compound of formula (IIIm) where all symbols are as defined above.

55. A pharmaceutical composition which comprises a compound of formula (IIIm)

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as defined in claim 53 and a pharmaceutically acceptable carrier, diluent, excipient or solvate.

56. A pharmaceutical composition as claimed in claim 55, in the form of a tablet, capsule, powder, syrup, solution or suspension.

25 57. A method for preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism comprising administering a compound of formula (IIIm) as defined in

claim 53 or a pharmaceutical composition as claimed in claims 55 or 56 to a patient in need thereof.

58. A method according to claim 57, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipideamia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive function in dementia and treating diabetic complications, osteoporosis, inflammatory bowel disease, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

59. A method according to claim 58, for the treatment or prophylaxis of disorders related to Syndrome X, which comprises administering an agonist of PPAR $\alpha$ , or PPAR $\gamma$  of formula (IIIm) or a mixture thereof.

60. A method of preventing or treating hyperlipemia, hypercholesterolemia, hyperglycemia, osteoporosis, obesity, glucose intolerance, leptin resistance, insulin resistance, or diseases in which insulin resistance is the underlying pathophysiological mechanism comprising administering a compound of formula (IIIm) as defined in

20 claim 53 or a pharmaceutical composition as claimed in claims 55 or 56 in combination/concomitant with HMG CoA reductase inhibitor, fibrates, nicotinic acid, cholestyramine, colestipol or probucol which may be administered together or within such a period as to act synergistically together to a patient in need thereof.

61. A method according to claim 60, wherein the disease is type II diabetes, impaired glucose tolerance, dyslipideamia, disorders related to Syndrome X such as hypertension, obesity, atherosclerosis, hyperlipidemia, coronary artery disease and other cardiovascular disorders, certain renal diseases including glomerulonephritis, glomerulosclerosis, nephrotic syndrome, hypertensive nephrosclerosis, retinopathy, nephropathy, disorders related to endothelial cell activation, psoriasis, polycystic ovarian syndrome (PCOS), useful as aldose reductase inhibitors, for improving cognitive function in dementia and treating diabetic complications, osteoporosis,

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inflammatory bowel diseases, myotonic dystrophy, pancreatitis, arteriosclerosis, xanthoma or cancer.

62. A method according to claim 61, for the treatment or prophylaxis of disorders related to Syndrome X, which comprises administering a compound of formula (IIIm) in combination with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol which may be administered together or within such a period as to act synergistically together.

63. A method of reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma, which comprises administering a compound of formula (IIIm) claimed in claim 53 or a pharmaceutical composition as claimed in claim 55 or 56 in combination/concomitant with HMG CoA reductase inhibitors, fibrates, nicotinic acid, cholestyramine, colestipol or probucol which may be administered together or within such a period as to act synergistically together to a patient in need thereof.

64. A method of reducing plasma glucose, triglycerides, total cholesterol, LDL, VLDL and free fatty acids in the plasma, which comprises administering a compound of formula (IIIm) claimed in claim 53 or a pharmaceutical composition as claimed in claim 55 or 56 to a patient in need thereof.